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Q4 The relation between 1st grade grey matter volume and 2nd grade 2 math competence

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ABSTRACT

Mathematical and numerical competence is a critical foundation for individual success in modern society yet the 18 neurobiological sources of individual differences in math competence are poorly understood. Neuroimaging re-9 search over the last decade suggests that neural mechanisms in the parietal lobe, particularly the intraparietal 20 sulcus (IPS) are structurally aberrant in individuals with mathematical learning disabilities. However, whether 21 those same brain regions underlie individual differences in math performance across the full range of math abil-22 ities is unknown. Furthermore, previous studies have been exclusively cross-sectional, making it unclear whether 23 variations in the structure of the IPS are caused by or consequences of the development of math skills. The present 24 study investigates the relation between grey matter volume across the whole brain and math competence longi-25 tudinally in a representative sample of 50 elementary school children. Results show that grey matter volume in the left IPS at the end of 1st grade relates to math competence a year later at the end of 2nd grade. Grey matter volume in this region did not change over that year, and was still correlated with math competence at the end of 28 2nd grade. These findings support the hypothesis that the IPS and its associated functions represent a critical poundation for the acquisition of mathematical competence. 30

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Q7 Introduction

Mathematical and numerical competence is a critical foundation for 37 individual success in modern society. Poor numeracy predicts higher 38 rates of unemployment, physical and mental illness, and even arrest 39 and incarceration (Bynner and Parsons, 1997; Parsons and Bynner, 40 2005), and yet, as many as one in four economically active individuals 41 42 fail to develop appropriate skills and are 'functionally innumerate' (Gross et al., 2009). Furthermore, the United States lags behinds its eco-43nomic peers in terms of math skills development, ranked 21st of 23 44 countries in a recent report by the Institute of Education Sciences 4546 (Goodman et al., 2014). In order to address this burgeoning problem, a deeper understanding of the developmental mechanisms underlying 47 math skills acquisition is needed. Characterization of the neural mecha-48 49 nisms underlying this process can contribute significantly to this understanding, and help to identify potential avenues for educational 50interventions and improved pedagogical methods. 51

Recent years have seen a growth in the number of neuroimaging studies investigating the development of math skills, yet in comparison to reading research for example, there remains a severe paucity of information. Consequently, knowledge regarding the neurocognitive factors underlying individual differences in math competence remains limited.

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http://dx.doi.org/10.1016/j.neuroimage.2015.08.046 1053-8119/© 2015 Elsevier Inc. All rights reserved. Nonetheless, a growing number of behavioral studies indicate that the 57 ability to represent and process nonsymbolic numerical magnitude is 58 a key cognitive foundation of math development. That cognitive mech- 59 anism is often referred to as the 'approximate number system' (ANS), 60 and is typically measured via performance on nonsymbolic numerical 61 comparison tasks (i.e. selecting which of two sets of dots is more nu- 62 merous). Performance on this task has been shown to correlate with 63 math ability in typically developing children (Halberda et al., 2008; 64 Mazzocco et al., 2011a, 2011b) and adults (Halberda et al., 2012), as **O8** well as being impaired in children with dyscalculia, a specific mathe- 66 matical learning disability (Mazzocco et al., 2011a, 2011b; Piazza et al., 67 2010). Neuroimaging studies in typically developing populations have 68 shown that the ANS is subserved by cortical mechanisms in the parietal 69 lobe, in particular, the intraparietal sulcus (IPS). This region is reliably 70 activated during nonsymbolic numerical comparison tasks in children 71 and adults (Ansari et al., 2006; Ansari and Dhital, 2006; Cantlon et al., 72 2006), and shows atypical activation in children with mathematical 73 learning disabilities (Price et al., 2007). The IPS has also been shown to 74 be actively involved in the processing of symbolic numerical magnitude 75 (i.e. selecting which of two Arabic digits is numerically larger) in typi-76 cally developing children and adults (Ansari et al., 2005; Pinel et al., 77 2001). Parietal brain activation during symbolic magnitude processing 78 has been related to math competence in typically developing children 79 (Bugden et al., 2012) and is atypical in children with mathematical 80 learning disabilities (Mussolin et al., 2009). Taken together, these 81

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findings suggest that the ability of IPS to process numerical magnitude is 82 83 a key foundation in the development of mathematical skills.

This critical role for the IPS in supporting the acquisition of math 84 85 skills is supported by structural as well as functional neuroimaging data. In line with the functional results reported above, several studies 86 have identified structural abnormalities, such as reduced grey matter 87 volume and abnormal sulcal geometry, in the IPS in children with math-88 89 ematical learning difficulties (Cappelletti and Price, 2014; Han et al., 90 2008; Isaacs et al., 2001; Lubin et al., 2013; Molko et al., 2003; Rotzer et al., 2007; Rykhlevskaia et al., 2009; Starke et al., 2013). These studies 09 92show that a failure to acquire age-appropriate math skills is associated with atypical structural integrity of the IPS, suggesting again that this re-93 gion is a key mechanism in the development of math competence. How-9495ever, there is a limit to the extent that evidence from atypically developing population can be extrapolated to typically developing pop-96 ulations. While the structure of the IPS may be atypical in children with 97 mathematical learning disabilities, it does not necessarily follow that in-98 dividual differences in the math skills of typically developing children 99 derive from the same source, as dyscalculia may represent a qualitative-100 ly distinct disorder rather than an extreme on a spectrum (Mazzocco 101 et al., 2011a). Furthermore, many of the studies listed above reported 102 data from populations with genetic syndromes such as Turner syn-103 104 drome (Molko et al., 2003) or atypical developmental environments such as prematurity/low birth-weight (Isaacs et al., 2001; Starke et al., 010 2013), and thus it is difficult to know whether the mathematical diffi-106 culties present in those populations mirror those in children with 107 'pure' math learning disabilities in their neurocognitive origins. There-108 109fore it is imperative that the role of the structure of the IPS in typical math development be established in a representative sample without 110 mathematical learning disabilities. 111

Only one study to date has assessed the association between individ-112 113 ual differences in neuroanatomical structure and math competence in a 114typically developing sample (Li et al., 2013). That study reported that math scores were positively correlated with grey matter volume in 115the left intraparietal sulcus, suggesting that the IPS is critical for typical 116 as well as atypical math development. However, that study employed a 117 region of interest (ROI) analysis approach whereby their analyses were 118 119 restricted solely to the IPS regions. Therefore it remains unknown whether other regions of the brain may show equally strong or even 120stronger, and by extension, more important relationships with individ-121 ual differences in math skills. 122

123 The present study addresses this open question by assessing the relation between grey matter volume across the whole brain and math 124 performance in a representative sample of 50 children without diagno-125sis of dyscalculia. In addition, the present study is the first to address this 126 issue with longitudinal data. Previous studies have all been cross-127128sectional, leaving open the question of whether individual differences in IPS structure are the cause or consequence of differences in math 129competence. The present study relates grey matter volume at the end 130of 1st grade to math competence at the end of 2nd grade, as well as 131 grey matter volume at the end of 2nd grade to math competence at 132133the same time point, thereby examining both longitudinal and concur-134rent relations. In so doing this study is, to the best of our knowledge, the first to ask (a) whether grey matter volume across the whole 135brain relates to math ability in a representative sample of children, 136and (b) whether any such relations are persistent over time. 137

Materials and methods 138

Participants 139

The present data were collected as part of a larger scale longitudinal 140 study investigating reading development. The current study comprises 141 those participants for whom standardized math scores were available. 142The following exclusion criteria were applied during the initial recruit-143 144 ment phase: 1) previous diagnosis of intellectual disability; 2) known, uncorrectable visual impairment; 3) documented hearing impairment 145 greater than or equal to 25 dB loss in either ear; 4) history of known 146 neurological disorders including epilepsy, spina bifida, cerebral palsy, 147 and traumatic brain injury; 5) current or past diagnosis of an autism 148 spectrum disorder; 6) treatment with any psychotropic medication -149with the exception of stimulant medications for ADHD; and 7) parental 150 report of significant symptoms of a severe psychiatric diagnosis includ- 151 ing major depression, bipolar disorders, or conduct disorder of note. In- 152 dividuals meeting criteria for ADHD, oppositional defiant disorder, 153 adjustment disorder, and mild depression were not necessarily exclud- 154 ed from participation. 155

The final sample for the current study comprised 50 students who 156 met the above inclusion criteria and completed standardized measures 157 of math achievement. Using the Edinburgh Handedness Inventory 158 (Oldfied, 1971), 33 students were classified as right-handed, 12 as am- Q11 bidextrous, and 5 as left-handed. Scanning sessions took place during 160 the summers following 1st grade and 2nd grade, 1 year apart (M = 1610.98, SD = 0.07). Two participants were missing WASI scores, but all 162 other measures for those participants were within 1 standard deviation 163 of the standardized test score means (M = 100, SD = 15). No partici- 164 pants were excluded based on IQ or reading achievement. Descriptive 165 and cognitive data for the sample are presented in Table 1. It should 166 be noted that participants in the current sample demonstrated a large 167 range in math scores. However, the mean scores were at or above aver- 168 age for Calculation, Applied Problems, and the composite measure. In Q12 addition, Kolgorov-Smirnoff tests show that for each of the measures 170 performance was normally distributed (p > .05 for each measure), sug- 171 gesting that the present sample comprised a representative range of 172 math performance levels. 173

Standardized cognitive measures used for analyses

Verbal ability

Due to the fact that in our sample WCJ-III Basic Reading was not nor- 176 mally distributed (Kolmogorov–Smirnov = .143, p = .012), the Pea- 177 body Picture Vocabulary Test IV, fourth edition (PPVT-4) was used as 178 a measure of verbal IQ to control for the influence of language ability 179 on math scores. In the PPVT, participants are asked to identify a picture 180 that corresponds to words of increasing difficulty. An abbreviated ver- 181 sion of the Wechsler Abbreviated Scale of Intelligence (WASI), including 182 the vocabulary and matrix reasoning subtests, was administered during 183 first grade as a metric of global IQ. 184

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Mathematical competence

Age normed standard scores from the Woodcock-Johnson III Tests of 186 Achievement Calculation and Applied Problems subtests were averaged 187 to create a composite measure of math ability (WCJ-III Math Compos- 188 ite). The Calculation subtest is an untimed, paper-and-pencil test that 189 includes age appropriate content beginning with basic number knowl- 190 edge and digit-based arithmetic. Applied Problems is an untimed verbal, 191

Table 1

Measure	1st grade ($N = 50$))	2nd grade ($N = 50$)		
	Μ	SD	Μ	SD	
Males/Females	19/31		19/31		
Age	7.44	0.34	8.41	0.35	
WCJ-III Calculation			102.92 (66-125)	13.01	
WCJ-III Applied Problems			108.74 (72-132)	13.74	
WCJ-III Math Composite			105.83 (72-125.5)	12.37	
WCJ-III Basic Reading			111.16 (71-131)	13.05	
WASI (abbreviated IQ)	113.50 (78–147) ^a	17.09			
PPVT-4 (verbal IQ)			112.46 (74-143)	15.35	

 a WASI-IQ was unavailable for 2 participants, but all other measures were within 1 SD of t1.12mean 02

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picture-based test that includes basic number knowledge, counting, and
arithmetic. Math competence scores were only available for 2nd grade
as they were not collected during the first year of the ongoing longitudinal study. Correlations between the above cognitive variables are reported in Table 2.

197 Neuroanatomical data acquisition and preprocessing

198 Image acquisition

199T1-weighted MRI was performed on a Philips Achieve 3 T scanner200with a 32-channel head coil. Magnetization Prepared Rapid Gradient**Q13**Recalled Echo (MP-RAGE; Mugler and Brookeman, 1990) anatomical202scans were acquired according to the following parameters:203 256×256 scan resolution; 170 slices; 1 mm slice thickness; 9.051 s204TR; 4.61 s TE; flip angle = 8°; voxel size 1 mm isotropic; and acquisition205time 274 s. Scans were oriented AC-PC.

206 Voxel-based morphometry

207Images were analyzed using SPM8 (Wellcome Trust Centre for Neuroimaging, http://www.fil.ion.ucl.ac.uk), on a MATLAB platform 208 (version 7.11, Mathworks, Natick, MA). Anatomical images for all anal-209yses were processed according to the VBM protocol described by 210Ashburner (2010) with the following specifications. T1-weighted struc-014 212tural scans were first segmented to obtain separate grey matter (GM), white matter (WM), and cerebral spinal fluid (CSF) images (Ashburner 015 and Friston, 2005). Second, a population-specific template was created 214using Diffeomorphic Anatomical Registration Through Exponentiated 215016 Lie Algebra (DARTEL) (Ashburner, 2007). Third, each subject's GM 217map was transformed to customized template space based on the 218sample of 50 participants and then normalized into MNI space by coregistering with the Montreal Neurological Institute (MNI152) brain 219template. The warped images were modulated by the Jacobian determi-220nants derived from DARTEL to obtain maps of GM volume maintaining 221 an isotropic voxel resolution of $1.0 \times 1.0 \times 1.0$ mm³. Two options 222 exist in SPM8 for handling the effects of warping of GM that affect sub-223sequent interpretation (Mechelli et al., 2005). One option is to leave 017 voxel intensities 'unmodulated' thereby preserving the concentration 225of GM in each voxel and changing the total amount of GM. Analyses 226on unmodulated images should be interpreted as findings related to 227GM concentration or density. The second option is to scale the intensity 228of GM by the Jacobian determinants derived from spatial normalization 229at each voxel, i.e., 'modulated' normalization. This procedure results in **O18** 019 preserved volumetric data (Ashburner and Friston, 2005). All subsequent analyses were performed on 'modulated' data utilizing the 232second option of normalization and thus the present results are 233interpreted in terms of regional GM volume. In the final stage of prepro-234cessing, the GM volume maps were smoothed with a full-width at half-235236maximum Gaussian kernel of 10 mm to normalize the data and accom-237modate minor variations in an individual's anatomy.

t2.1 Table 2

	1	2	3	4
1. WCJ-III Composite				
2. WCJ-III Calculation				
	.921**			
3. WCJ-III Applied Problems		.712**		
	.929**			
4. PPVT-4		.456**	.607**	
	.576**			
5. WCJ-III Basic Reading		.475**	.712.**	.617**
	.645**			

t **Q3** ** Indicates *p* < .001

Analyses

Math competence and whole brain grey matter volume

To investigate whether regional grey matter volume across the 240 whole brain at the end of 1st grade and 2nd grade relate to individual 241 differences in math achievement scores at the end of 2nd grade, we 242 used two multiple linear regression models relating WCJ-III Math Com- 243 posite scores to VBM derived grey matter volume maps at 1st grade and 244 2nd grade respectively. Age at time of scan, sex, global brain volume 245 (WM + GM + CSF), and PPVT-4 (2nd grade) were included as covari- 246 ates in the model to control for anatomical differences related to age, 247 sex, overall brain volume, and verbal ability. The regression analysis 248 was run on the whole brain with an absolute threshold mask of 0.01. 249 A cluster level correction threshold of p < 0.05 was applied using the 250 REST AlphaSim correction (uncorrected p < .0005, minimum cluster 251 threshold: 680 voxels 1st grade, 587 voxels 2nd grade). AlphaSim is a 252 non-parametric and non-isotropic, simulation-based method for deter- 253 mining the family-wise error threshold (http://restfmri.net/forum/ 254 REST). 255

Math competence and changes in whole brain grey matter volume 256

In addition to testing whether grey matter volume in year 1 or year 2 257 relates to math ability in year 2, we tested whether *change* in grey mat-258 ter volume between years 1 and 2 relates to math performance at year 2. 259 To this end, voxel-wise change in the grey matter volume for each par-260 ticipant was measured by subtracting the grey matter volume image at 261 1st grade from that at 2nd grade using the ImCalc utility (http://262 robjellis.net/tools.html) in SPM8. The correlation between this change 263 metric and grey matter volume at 1st grade was non-significant 264 (r = -.05, p = .73), indicating that variance in change scores was Q20 not driven by values at baseline. The resulting individual subject maps 266 detailing the voxel-wise change in grey matter volume were then sub-267 jected to the same regression analysis as described in the above analy-268 ses, with standardized math performance as the covariate of interest, 269 and age, sex, and PPVT-4 as covariates of non-interest. 270

Region-of-interest (ROI) analysis

To eliminate the possibility that different individuals account for the 272 results at 1st grade and 2nd grade, and to establish the stability of grey 273 matter volume within the left IPS, a correlation between the mean re-274 gional grey matter volumes per voxel across both years was performed. 275 ROIs were defined based on the clusters identified in the primary VBM 276 analyses (1st grade's ROI peak voxel coordinates: x = -33, y = -60, 277 z = 50, cluster size: 1041 voxels; 2nd grade's ROI peak voxel coordi-278 nates: x = -33, y = -61, z = 50, cluster size: 675 voxels). For each 279 ROI, the mean grey matter volume per voxel was extracted from all par-280 ticipants using the MarsBaR region of interest toolbox (version 0.44; 281 http://marsbar.sourceforge.net/), with proportional scaling applied. 282

Results

Math competence and whole brain grey matter volume

The multiple regression analysis predicting 2nd grade math scores 285 from grey matter volume in 1st grade identified one cluster in the left 286 IPS after controlling for age at time of scan, sex, and verbal IQ (peak 287 MNI coordinate: x = -33, y = -60, z = 50, t = 4.80, 1041 voxels, 288 p < .05 cluster corrected) (Fig. 1a). The regression analysis predicting 289 2nd grade math scores from 2nd grade grey matter volume identified 290 an almost identical cluster in the left IPS with the same control variables 291 (peak MNI coordinate: x = -33, y = -61, z = 50, t = 4.33, 675 voxels, 292 p < .05 cluster corrected) (Fig. 1b). The majority of each cluster was 293 identified as hIP3 within the IPS using the SPM8 Anatomy Toolbox 294

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Fig. 1. Significant clusters of grey matter related to math in 1st grade (A) and 2nd grade (B) after controlling for age at time of scan, sex, and PPVT-4.

021 v2.15 (Eickhoff et al. 2005) with the cluster extending into nearby pari-296 etal regions (Table 3). To ensure that the results above were not driven by the inclusion of PPVT as a covariate, we conducted the analysis with 297math competence as the sole cognitive predictor. The relation between 298grey matter volume in the left IPS region and math competence 299 remained significant (p = .0005 uncorrected, p < .05 cluster level 300 corrected). The same was true of grey matter at 2nd grade, albeit at a 301 slightly lower (but widely used) uncorrected threshold (p = .005 un-302 corrected, p < .05 cluster level corrected). 303

Our main analysis used a composite measure of math competence to 304 capture mathematical/computational processes over and above those 305 306 specific to a single subtest (e.g. digit processing for calculation vs verbal 307 processing for applied problems). However, we were additionally inter-308 ested in whether the two subtests were associated differentially with grey matter volume across the whole brain. Therefore, we conducted 309 two additional analysis using Woodcock-Johnson Calculation and Ap-310311 plied Problems as the dependent variables respectively. These separate analyses revealed that when age at time of scan, sex, global brain vol-312 ume (WM + GM + CSF), and PPVT-4 (2nd grade) were included as co-313 variates in the model, WCJ-Calculation was related to increased grey 314 matter in the region of the superior temporal/angular (-47, -54,022 9) gyrus for both 1st and 2nd grades (1st grade = 555 voxels, 2nd 316 grade = 503 voxels. p = .0005 uncorrected, p < .05 cluster level 317 corrected). The left IPS region reported in the main analysis was present 318 but only survived cluster-level (p < .05) correction at a lower uncorrect-319 320 ed threshold of p = .005 for year 1, and did not survive correction for 321 year 2. The same analysis using Applied Problems revealed an associa-322 tion with the same left IPS region reported in the main analysis for both 1st and 2nd grade (1st grade = 922 voxels, 2nd grade = 921 323 voxels. p = .0005 uncorrected, p < .05 cluster level corrected). 324

Math competence and changes in whole brain grey matter volume 325

No suprathreshold clusters were found at a threshold of p < .0005 326 (uncorrected), or at a more liberal uncorrected threshold of p < .005. 327 Therefore cluster level correction was not applied. In other words, indi- 328 vidual differences in math performance at 2nd grade were not predicted 329 by changes in grey matter volume in the preceding year in any brain 330 region. 331

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ROI analysis

Mean grey matter volume in the left IPS regions identified in the 1st 333 and 2nd grade analyses showed a strong positive correlation with each 334 other (r = .955, p < .001). This suggests that the mean grey matter vol-335 ume within these regions remained relatively stable within a one-year 336 period. More importantly, it indicates that the results of 1st grade and 337 2nd grade analyses were likely to be accounted for by the same individ-338 uals (Table 4).

Discussion

The current study is the first to investigate the longitudinal relation- 341 ship between grey matter volume across the whole brain and math 342 competence in children without mathematical learning difficulties. 343 Testing for a relation between math competence at the end of 2nd 344 grade and grey matter volume at the end of 1st grade, we show that 345 across the whole brain, only left intraparietal sulcus (IPS) grey matter 346 volume relates to math competence at the end of 2nd grade. Grey matter volume in the same region at the end of 2nd grade related to concur-348 rent math competence, and no region of the brain showed a relation 349

t3.2	VBM results for 1st and 2nd grades.								
t3.3	Grade (at scan)	Hemisphere	Peak MNI (x y z)	Cluster size	Т	Z	p corrected	BA	Anatomical description
t3.4	1st	Left	(-33 - 60 50)	1041	4.80	4.29	< 0.05	7	IPS
t3.5	2nd	Left	(-33-6150)	675	4.33	3.94	< 0.05	7	IPS
		``							

t3.6 IPS (intraparietal sulcus).

Table 3

t3.1

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t4.1 Table 4

t4.2 Cluster details for 1st and 2nd grades.

	Number of voxels	% of voxels in cluster	Anatomical description	% Coverage of anatomical description area
Cluster at 1st grade	605	66.8	Left hID3 (IDS)	20.3
(1041 voxels)	264	25.4	Left 7A	26
(To Tr Volicio)	39	3.7	Left hIP1 (IPS)	2.0
	39	3.7	Left PGa (IPL)	0.8
Total	1037	99.6		
Cluster at 2nd grade	503	74.5	Left hIP3 (IPS)	14.7
(675 voxels)	138	20.4	Left 7A (SPL)	1.4
. ,	20	3.0	hIP1 (IPS)	1.0
	12	1.8	PGa (IPL)	0.2
Total	673	99.7		

t4.17 (IPS) intraparietal sulcus, (hIP3) subregion of IPS, (7A) Brodmann area 7A, (hIP1) subret4.18 gion of the IPS, (PGa) subregion of the superior parietal lobule.

between change in grey matter volume from year 1 to year 2 and math
 competence. These results indicate a significant and stable role for
 the left IPS in the development of individual differences in math
 competence.

The present results compliment a growing body of literature sug-354 355 gesting that the IPS is a critical neural foundation for the development 356 of math competence. Previous studies have shown that the IPS has atypical structural properties in children with mathematical learning dis-357 abilities (Starke et al., 2013; Lubin et al, 2013; Rykhlevskaia et al., 024 2009; Isaacs et al., 2001; Molko et al., 2003). Furthermore, the activation 359360 of this region during numerical processing tasks is atypical in children with dyscalculia (Price et al., 2007; Mussolin et al., 2010). However, it 361 cannot be assumed that neuroanatomical mechanisms that distinguish 362 children with math learning disabilities from their typically developing 363 364 peers are the same mechanisms that underlie individual differences in 365 typically developing math competence. To the best of our knowledge, 366 only one study to date has investigated the relation between grey matter volume and math competence in typically developing children (Li 367 et al., 2013), showing that math competence correlated with grey mat-368 ter volume in the left IPS. However, that study employed a region of in-369 370 terest analysis, excluding regions outside the bilateral IPS from analysis, leaving open the question of whether grey matter volume in the IPS is in 371 fact the most significant neuroanatomical predictor of math compe-372tence. Indeed, several functional imaging studies have shown that 373 374 while functional activation of the IPS during numerical magnitude processing predicts math ability (Bugden et al., 2012), activation of other 375 frontal and parietal regions during arithmetic tasks, in particular the 376 left angular and supramarginal gyri, correlate with math ability 377 (Ansari et al., 2011; Price et al., 2013). This distinction further highlights 378 379 the need to explore the whole brain as opposed to a priori restricted regions when investigating the relation between brain structure and math 380 381 competence.

The present results suggest that in terms of structural neuroanatomy, when considering math competence broadly across multiple subtests, the IPS demonstrates the most significant association with math competence. Structural properties of the left superior temporal/angular gyrus, on the other hand, appear to have an association with calculation specifically.

The left IPS region identified in this study has previously been asso-388 389 ciated at the cognitive level with numerical magnitude processing. Activation in this region is often observed during numerical comparison 390 tasks using both Arabic digits (Bugden et al., 2012; Mussolin et al., 391 2010; Pinel et al., 1999) and nonsymbolic quantities (Ansari and 392 Dhital, 2006; Cantlon et al., 2006; Piazza et al., 2004). Therefore, at a 393 basic level the current findings could be seen to lend support to the hy-394pothesis that numerical magnitude system or 'approximate number 395 system' (ANS) is a critical foundation for the development of math com-396 petence. However, more recent evidence suggests that some degree of 397 398 hemispheric lateralization may be at play in the intraparietal sulcus, whereby the left IPS is engaged by symbolic magnitude processing 399 while the right IPS is more engaged by nonsymbolic magnitude process- 400 ing (Ansari, 2008; Holloway et al., 2013; Vogel et al., 2015). In addition, 401 a number of recent studies have suggested that symbolic magnitude 402 processing is a stronger predictor of math skills than nonsymbolic mag- 403 nitude processing (De Smedt et al., 2013). Therefore, the current find- 404 ings suggest that the neural mechanisms underlying the processing of 405 symbolic numerical magnitude in particular are the critical foundation 406 for the development of math competence. Whether this symbolic mag- 407 nitude processing represents an interaction between the ANS and sym- 408 bolic systems, or whether it is fully abstracted from the ANS remains an 409 open empirical question. The left angular gyrus, on the other hand, has 410 previously been more typically associated with calculation fluency 411 (Delazer, 2003; Grabner, Ansari, et al., 2009; Grabner, Ischebeck, et al., 412 2009). The present results provide further evidence for the role of this 413 region in calculation as a specific sub-domain of mathematical 414 competence 415

Findings relating basic numerical magnitude processing to math de- 416 velopment has led some researchers to conclude that improving basic 417 magnitude processing ability may have beneficial implications for 418 math competence (Lindskog et al., 2013; Park and Brannon, 2013). 419 The current data suggests that this approach may be productive, as 420 the structural integrity of the IPS appears to be a key foundation for 421 math competence. However, the lack of change in grey matter volume 422 in that region over a year of schooling suggests that interventions 423 targeting that system may need to be enacted early in development, at 424 least prior to 1st grade, as by the end of 1st grade this neural system 425 may no longer be malleable. Furthermore, it should also be noted that 426 changes in functional activation over development are not always mir- 427 rored by concomitant changes in grey matter structure (Rivera et al., 428 2005) and so the extent to which the neural systems underlying numer- 429 ical magnitude processing are subject to sensitive periods remains an 430 open empirical question. It should also be noted as a limitation of the 431 present study that math competence measures were only available for 432 2nd grade as they were not collected during the first year of the longitu- 433 dinal study. This fact restricts our ability to draw causal inferences from 434 the current data as a true bidirectional relationship could not be 435 established. Future research comprising both neuroanatomical and 436 math competence data from two time points is needed to further eluci- 437 date the question of causality. 438

In summary, the present results show that grey matter volume in the 439 left IPS at the end of 1st grade is related to math competence a year later 440 at the end of 2nd grade. Grey matter volume in this region did not 441 change over that year, and was still correlated with math competence 442 at the end of 2nd grade. These findings support the hypothesis that 443 the IPS and its associated functions represent a critical foundation for 444 the acquisition of mathematical competence. 445

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